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C. H. BOEHRINGER SOHN  
INGLEHEIM AM RHEIN

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COMBINED INTELLIGENCE OBJECTIVES  
SUB COMMITTEE





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C. H. BOEHRINGER SOHN

INGLEHEIM AM RHEIN, GERMANY

16 May 1945.

Reported By

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C.M. Hq

10 July 1945.

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COMBINED INTELLIGENCE OBJECTIVES SUB-COMMITTEE  
G-2 Division, SHAEF (Rear) APO 413

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C. H. BOEHRINGER SOHN  
INGLEHEIM AM RHEIN, GERMANY

1. INTRODUCTION

This plant is located about twenty miles south west of Wiesbaden. The general condition of the plant was found to be good - thirty five shells had caused some damage but mostly to buildings, not to essential process equipment. The plant had been unable to do anything during the Occupation although one month's coal was in the bins and military government approved orders had been received. Two thirds of the plant was occupied as troop billets and fear was expressed by the management that delicate laboratory apparatus had been damaged and stocks of pharmaceuticals removed to locations unknown. The management and the investigators were denied admission to these parts. Two thousand five hundred people were normally employed. Small branch factories, sales offices etc., were located at Hamburg, Wien, Biberach, Wurtemberg. The main plant was at Niederingleheim. Dr. Boehringer, Dr. Strobell and Dr. Dethloff were interviewed.

2. PRODUCTS

The factory was solely devoted to making pharmaceuticals and closely related materials from natural products. Most chemicals required were secured from I.G. Farbenindustrie A.G. Most processes consisted of entirely normal extractions.

A partial list of products is: -

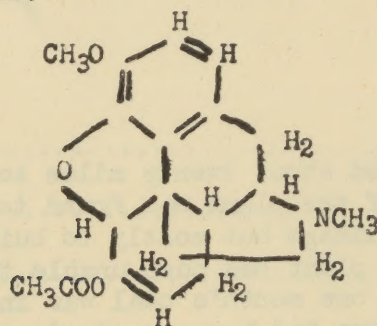
Tartaric acid & salts  
Lactic acid & salts  
Citric acid & salts  
Alkaloids of vegetable origin  
Strychnine  
Atropine  
Scopolamine  
Emetine  
Esserine

Phenylquinoline carboxylic  
acid  
Cholic acid & salts  
Cholesterol  
Ergosterol  
Calcium Gluconate  
Opium appilaries (Hamburg)  
Baking auxiliaries  
Natural caffeine  
Synthetic caffeine

The baking auxiliaries were mainly to inhibit mold growth on aging. Calcium acetate produced from pure acetic acid was an important ingredient. It was believed that calcium propionate had been used similarly in America.

The following list comprises speciality pharmaceuticals:

- a. Acedicon, a cough remedy for severe cases bronchitis, tuberculosis.



- b. Adrianol-Emulsion, Levo-Meta-Methylaminoethanolphenol-chlorhydrate AN, isomer of adrenalin and sympatol. The emulsion was very stable and consisted of 0.25% adrianol in paraffin oil preserved with sodium benzoate. It was used similarly to adrenalin.
- c. Aludrin, Sulfuric acid salt of dioxyphenylethanol isopropylamine, which is chemically similar to adrenalin with the substitution of an isopropyl group for the methyl group next to the nitrogen. It was used in treating bronchial asthma. This was also spelled Aleudrin.
- d. Bilival, a preparation containing 25% lecithin and 75% sodium cholate. It was used in treatment of the liver.
- e. Codyl-sirup, one teaspoon contains .004 g codeine hydrochloride, about .002 g narcotin and .001 g papaverine. A cough remedy.



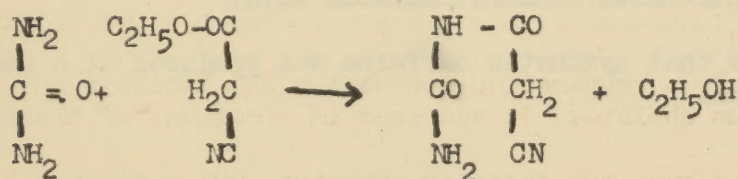
- f. Euxanthin, one pill contains 0.1 g catechol and 0.15 g theophylline sodium acetate. It was a preparation for the treatment of the heart.
- g. Lacalut, a tooth powder made from aluminum lactate with a medicinal as well as a cleansing action.
- h. Lobelin "Ingelheim" (Lobeton), a synthetic alkaloid with the constitution of the natural product from the lobelia. It was used in a similar manner to the natural product for nervous disorders connected with the breathing system.
- i. Lobelin-Sympatol (Lobesym), a combination of Lobelin and Sympatol.
- j. Sympatol, P-Methylaminoethanolphenol prepared as the acetic acid salt. It was stable in air and to light and heat. It was used in the treatment of the heart and circulation particularly after an infectious disease. This pharmaceutical was regarded as the most important one made by Boehringer and Sohn. They made two thousand five hundred Kg per month.

It was stated specifically that antimalarials were not made.

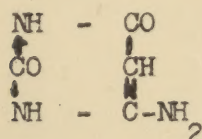
In normal times Boehringer extracted theobromine from cacao wastes imported from Holland and shipped into Hamburg. The theobromine was methylated at Ingelheim to the trimethyl derivative, caffeine. Because of the stoppage of imports of cacao due to the war it became necessary to synthesize caffeine.

Boehringer's production of synthetic caffeine was made by the standard Traube synthesis.

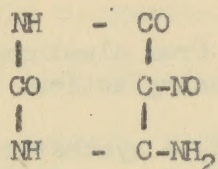
Ethyl cyanoacetate was reacted with an equimolar quantity of urea in the presence of sodium methylate.



The cyanacetyl urea rearranged to:

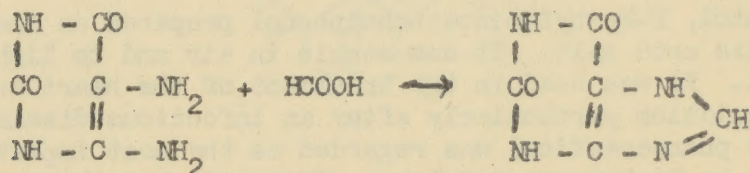


which was reacted with a molar quantity of  $\text{NaNO}_2$  to yield the nitroso compound -



This was reduced with powdered zinc, using 125% of theory, to yield the 4,5- diamino uracil which was isolated as the sulfate salt.

The diamino uracil was then reacted with an excess of formic acid, the acid also being used as the solvent medium for the reaction -



Finally the xanthine was methylated using 110% of theory of methyl chlorides at 10 atmospheres pressure in the presence of NaOH to yield 1,3,7- trimethyl xanthine or caffeine.

The overall yield was 40% of theory based on ethyl cyano acetate. While this is quite low it should be remembered that a 90% yield in each step would give an overall yield of only 64%. The poorest yields occurred in the first, ring closure, reaction and in the final methylation step. Here the alkaline conditions necessary to carry out the main reaction result also in a side reaction with the caffeine or the intermediate products.

The maximum rate of production was 5000 kg per month. It was stated that this was the only plant in Germany which produced synthetic caffeine. The ethyl cyanoacetate was prepared at Boehringer from purchased monochloroacetic acid.

It was stated that synthetic caffeine was produced at a cost of 40 RM per kilogram.



### 3. RECOMMENDATION

This plant might aid in supplying pharmaceuticals during reconstruction. The management were helpful in the investigation and furnished pamphlets and sales literature etc. It is recommended that a pharmaceutical team investigate this target further, with particular attention to new methods of production.







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